PATENT

Attorney Docket No.: 00537/163002

IN RE APPLICATION OF:

M. A. CAWTHORNE et al.

APPLICATION NO.: 09/423,683

FILED: MARCH 20, 2000

FOR: METHOD AND COMPOSITIONS FOR

TREATING HYPERLIPIDEMIA AND

OTHER CONDITIONS

EXAMINER: A. Mohammed

ART UNIT: 1653

I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Assistant Commissioner of Patents, Washington, D.C. 20231.

Date of Deposit: June 17, 2002

Kare Luck

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CLEAN VERSION OF PENDING CLAIMS

:

1. (Amended) A method of treating hyperlipidemia in a patient in need of such treatment, said method comprising administering a therapeutically effective amount of a somatostatin type-5 receptor agonist to said patient.



- 6. (Amended) Α method of owering the amount. triacylglycerols, glycerol or cholesterol in the blood of a patient in need of such lowering, said method comprising administering therapeutical y effective a amount somatostatin type-5 receptor aganist to said patient.
- 8. A method of claim 6, wherein said method comprises lowering the amount of triacylglycerols in said patient.
- 18. A method of claim 6, wherein said method comprises lowering the amount of cholesterol in said patient.
- B3
- 32. (New) A pharmaceutical composition for the treatment of hyperlipidemia in a patient in need thereof, comprising a therapeutically effective amount of a somatostatin type-5 receptor agonist, wherein said therapeutically effective amount

is an amount that is effective for the treatment of hyperlipidemia in said patient.

- 33. (New) A pharmaceutical composition according to claim 32, wherein said somatostatin type-5 receptor agonist is a somatostatin type-5 receptor selective agonist.
- 34. (New) A pharmaceutical composition according to claim 32, wherein said somatostatin type-5 receptor agonist has a Ki of less than 2 nM for the somatostatin type-5 receptor.
- 35. (New) A pharmaceutical composition according to claim 32, wherein said somatostatin type-5 receptor agonist has a Ki for the type-5 somatostatin receptor that is at least 10 times less than its Ki for the somatostatin type-2 receptor.
- , 36. (New) A pharmaceutical composition according to claim 32, wherein said somatostatin type-5 receptor agonist is:

 $H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2$, where a disulfide bond exists between the free thiols of the two Cys residues, or $H-D-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2$.

37. (New) A pharmaceutical composition according to claim 32, wherein said somatostatin type-5 receptor agonist is:

 $ext{H-Cys-Phe-D-Trp-Lys-Ser-Phe-Cys-NH}_2$;

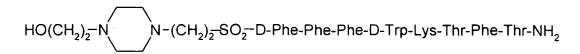
H-Cys-Phe-Tyr-D-Trp-Lys-Thr-Phe-Cys-NH2;

H-Cys-Phe-Tyr(I)-D-Trp-Lys-Thr-Phe-Cys-NH2;

wherein a disulfide bond exists between the free thiols of the two Cys residues in each of the foregoing agonists;

$$\label{eq:hocho} \text{HO(CH}_2)_2 - \text{N} - (\text{CH}_2) - \text{CO-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH}_2$$

or



- 38. (New) A pharmaceutical composition for lowering the amount of triacylglycerols in the blood of a patient in need of such lowering, comprising a therapeutically effective amount of a somatostatin type-5 receptor agonist, wherein said therapeutically effective amount is an amount that is effective for lowering the amount of triacylglycerols in the blood of said patient.
- 39. (New) A pharmaceutical composition according to claim 38, wherein said somatostatin type-5 receptor agonist is a somatostatin type-5 receptor selective agonist.
- 40. (New) A pharmaceutical composition according to claim 38, wherein said somatostatin type-5 receptor agonist has a Ki of less than 2 nM for the somatostatin type-5 receptor.
- 41. (New) A pharmaceutical composition according to claim 38, wherein said somatostatin type-5 receptor agonist has a Ki for the type-5 somatostatin receptor that is at least 10 times less than its Ki for the somatostatin type-2 receptor.
- 42. (New) A pharmaceutical composition according to claim 38, wherein said somatostatin type-5 receptor agonist is:

 $\label{eq:he-phe-D-Trp-Lys-Thr-Phe-Cys-NH2} \mbox{, where a disulfide bond exists between the free thiols of the two Cys residues, or $$H-D-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH2.}$

43. (New) A pharmaceutical composition according to claim 38, wherein said somatostatin type-5 receptor agonist is:

H-Cys-Phe-Phe-D-Trp-Lys-Ser-Phe-Cys-NH2;

H-Cys-Phe-Tyr-D-Trp-Lys-Thr-Phe-Cys-NH2;

H-Cys-Phe-Tyr(I)-D-Trp-Lys-Thr-Phe-Cys-NH2;

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wherein a disulfide bond exists between the free thiols of the two Cys residues in each of the foregoing agonists;

$$HO(CH_2)_2 - N$$
 $N-(CH_2) - CO-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH2$

or

$$\mathsf{HO}(\mathsf{CH}_2)_2^-\mathsf{N} - (\mathsf{CH}_2)_2^-\mathsf{SO}_2^-\mathsf{D}\text{-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH}_2$$

- 44. (New) A pharmaceutical composition for lowering the amount of glycerol in the blood of a patient in need of such lowering, comprising a therapeutically effective amount of a somatostatin type-5 receptor agonist, wherein said therapeutically effective amount is an amount that is effective for lowering the amount of glycerol in the blood of said patient.
- 45. (New) A pharmaceutical composition according to claim 44, wherein said somatostatin type-5 receptor agonist is a somatostatin type-5 receptor selective agonist.
- 46. (New) A pharmaceutical composition according to claim 44, wherein said somatostatin type-5 receptor agonist has a Ki of less than 2 nM for the somatostatin type-5 receptor.
- 47. (New) A pharmaceutical composition according to claim 44, wherein said somatostatin type-5 receptor agonist has a Ki for the type-5 somatostatin receptor that is at least 10 times less than its Ki for the somatostatin type-2 receptor.
- 48. (New) A pharmaceutical composition according to claim 44, wherein said somatostatin type-5 receptor agonist is:

 $H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2$, where a disulfide bond exists between the free thiols of the two Cys residues, or $H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2$.



49. (New) A pharmaceutical composition according to claim 44, wherein said somatostatin type-5 receptor agonist is:

H-Cys-Phe-Phe-D-Trp-Lys-Ser-Phe-Cys-NH2;

H-Cys-Phe-Tyr-D-Trp-Lys-Thr-Phe-Cys-NH2;

H-Cys-Phe-Tyr(I)-D-Trp-Lys-Thr-Phe-Cys-NH2;

wherein a disulfide bond exists between the free thiols of the two Cys residues in each of the foregoing agonists;

$$HO(CH_2)_2$$
-N- (CH_2) -CO-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂

or

$$\mathsf{HO}(\mathsf{CH}_2)_2^-\mathsf{N} - (\mathsf{CH}_2)_2^-\mathsf{SO}_2^-\mathsf{D}\text{-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH}_2$$

- 50. (New) A pharmaceutical composition for lowering the amount of cholesterol in the blood of a patient in need of such lowering, comprising a therapeutically effective amount of a somatostatin type-5 receptor agonist, wherein said therapeutically effective amount is an amount that is effective for lowering the amount of cholesterol in the blood of said patient.
- 51. (New) A pharmaceutical composition according to claim 50, wherein said somatostatin type-5 receptor agonist is a somatostatin type-5 receptor selective agonist.
- 52. (New) A pharmaceutical composition according to claim 50, wherein said somatostatin type-5 receptor agonist has a Ki of less than 2 nM for the somatostatin type-5 receptor.
- 53. (New) A pharmaceutical composition according to claim 50, wherein said somatostatin type-5 receptor agonist has a Ki

for the type-5 somatostatin receptor that is at least 10 times less than its Ki for the somatostatin type-2 receptor.

54. (New) A pharmaceutical composition according to claim 50, wherein said somatostatin type-5 receptor agonist is:

 $H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH_2$, where a disulfide bond exists between the free thiols of the two Cys residues, or $H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH_2$.

55. (New) A pharmaceutical composition according to claim, wherein said somatostatin type-5 receptor agonist is:

H-Cys-Phe-Phe-D-Trp-Lys-Ser-Phe-Cys-NH2;

H-Cys-Phe-Tyr-D-Trp-Lys-Thr-Phe-Cys-NH2;

H-Cys-Phe-Tyr(I)-D-Trp-Lys-Thr-Phe-Cys-NH2;

wherein a disulfide bond exists between the free thiols of the two Cys residues in each of the foregoing agonists;

$$HO(CH_2)_2 = N - (CH_2) - CO - D$$
-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂

or

$$\label{eq:hocho} \text{HO(CH}_2)_2 = \text{N} - (\text{CH}_2)_2 - \text{SO}_2 - \text{D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH}_2$$